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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,891	12/02/2003	John Humphreys	3220-73872	3355
23643	7590	11/21/2005	EXAMINER	
BARNES & THORNBURG 11 SOUTH MERIDIAN INDIANAPOLIS, IN 46204			VENCİ, DAVID J	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/725,891	Applicant(s) HUMPHREYS, JOHN	
	Examiner David J. Venci	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on August 30, 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-13, 15-18, 20, 21, 30 and 31 is/are pending in the application.
- 4a) Of the above claim(s) 1-4, 6-12 and 30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13, 15-18, 20, 21 and 31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-4, 6-13, 15-18, 20, 21, 30 and 31 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Examiner acknowledges Applicant's reply, filed August 30, 2005. Currently, claims 13, 15-18, 20-21 and 31 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Newly submitted claim 30 is directed to an invention that is independent and patentably distinct from the invention originally elected. Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-4, 6-12 and 30, drawn to methods for protein quantification, classified in class 435/7.92, for example.
- II. Claims 13, 15-18, 20-21 and 31, drawn to a method of detecting a P450 protein, classified in class 435/69.7, for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are independent and patentably distinct. Inventions are independent and patentably distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different modes of operation because Invention I requires a substrate, while Invention II requires a P450 protein comprising an epitope.

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For the reasons given, supra, Inventions I and II are distinct. In addition, examination burden is established because a search for prior art required for Invention I does not require a search for prior art for Invention II. For example, examination of Invention I requires a search for prior art related to heterogeneous, solid phase assays, which examination of Invention II requires a search for prior art related to a specific enzyme class.

Examiner acknowledges Applicant's request to rejoin the invention of Invention I, claims 1-4, 6-12 and 30. Applicant argues, "examination of the generic claims [i.e. Invention I] with the present P450 species claims [i.e. Invention II] is believed not to constitute an additional burden to the Examiner since the patentability of [Invention I and Invention II] rest on the same principle." Examiner respectfully disagrees for the reasons set forth supra.

For the foregoing reasons, the requirement for restriction for examination purposes is considered proper and is made FINAL.

Since applicant has received an action on the merits for originally presented Invention II, this invention is constructively elected by original presentation for prosecution on the merits. Accordingly, newly added claim 30 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

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Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Specifically, claim 16 is amended to add the sequence Asp-Tyr-Lys-Asp-Asp-Asp-Lys. However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g).

Applicant is requested to return a copy of the attached Notice to Comply with the response. Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio
(<http://www.uspto.gov/ebs/efs/downloads/documents.htm>), EFS Submission
User Manual - ePAVE)

2. Mailed to:

**U.S. Patent and Trademark Office
Box Sequence, P.O. Box 2327
Arlington, VA 22202**

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, Examiner is unable to locate antecedent support for a "picomolar" concentration parameter in the specification, as originally filed. Thus, a "picomolar" concentration parameter appears to be new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13, 15 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Yabusaki et al. (US 5,436,159).

Yabusaki et al. describe a method for quantifying a P450 protein (see col. 7, line 67, “[d]etermination of expression amount”) comprising: providing a recombinant P450 protein (see col. 7, line 67-68, “chimeric fused protein of P-450 and reductase”) comprising an epitope (see col. 7, line 68, “reductase”); contacting the P450 protein with a labeled ligand that directly binds to the epitope (see col. 8, lines 28-29, “anti-reductase antibody”); directly detecting the labeled ligand (see col. 8, line 36, “[¹²⁵I]protein A”); and quantifying the detectably labeled protein (see sentence bridging cols. 8-9, “6-7X10⁴ molecules of heme-containing P-450/reductase chimetic fused proteins per cell”).

Claim Rejections - 35 USC § 103

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yabusaki et al. (US 5,436,159) in view of Hopp & Prickett (US 4,851,341).

Yabusaki et al. describe a method for quantifying a P450 protein as substantially described, *supra*, and incorporated herein.

Yabusaki et al. do not describe an epitope comprising the sequence Asp-Tyr-Lys-Asp-Asp-Asp-Lys (hereinafter "FLAG[®] tag").

However, Hopp & Prickett describe the use of FLAG[®] tags (see Abstract) for purifying (see Title) and detecting (see col. 6, lines 27-28, "Western immunoblots") recombinant proteins.

Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method for quantifying a P450 protein, as described by Yabusaki et al., with a FLAG[®] tag because Hopp & Prickett developed a system that "provides superior identification and purification performance" (see col. 2, lines 56-57) while avoiding "use of affinity elution methods employing high salt, low pH, or chaotropic agents, which may be irreversibly denaturing" (see col. 3, lines 23-25).

Claims 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yabusaki et al. (US 5,436,159) and Hopp & Prickett (US 4,851,341), as applied to claims 13 and 15-16, and further in view of Kay (US 3,789,116).

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Yabusaki et al. and Hopp & Prickett describe a method for quantifying a P450 protein as described, *supra*, and incorporated herein. In addition, Hopp & Prickett describe the preparation of monoclonal antibodies against FLAG[®] tags (see col. 4, lines 40+).

Yabusaki et al. and Hopp & Prickett do not describe a fluorophore-conjugated antibody.

However, Kay describes the use of fluorescent chemicals for labeling antibodies (see Abstract).

Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method for quantifying a P450 protein, as described by Yabusaki et al. and Hopp & Prickett, with a fluorophore-conjugated antibody because Kay discovered antibody reagents "having superior sensitivity" (see col. 1, line 66) and "excellent fluorescent characteristics including both brightness and color" (see col. 2, lines 20-24).

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yabusaki et al. (US 5,436,159), Hopp & Prickett (US 4,851,341), and Kay (US 3,789,116) as applied to claims 13 and 18, and further in view of Amersham Pharmacia Biotech, *What's new*, Life Science News 4 (2000), available at <<http://www4.amershambiosciences.com>>.

Yabusaki et al., Hopp & Prickett, and Kay describe a method for quantifying a P450 protein as substantially described, *supra*, and incorporated herein.

Yabusaki et al., Hopp & Prickett, and Kay do not describe a phosphor autoradiography imager.

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However, Amersham Pharmacia Biotech teaches the use of a phosphor autoradiography imager (see Title, "Typhoon 860 Variable Mode Imager") for scanning gels, blots and phosphor screens (see seventh bullet). Therefore, it would have been obvious for a person of ordinary skill in the art to perform the method of quantifying a P450 protein, as taught by Yabusaki et al., Hopp & Prickett, and Kay, with a phosphor autoradiography imager because Amersham Pharmacia Biotech discovered that phosphor autoradiography imagers enable "direct chemiluminescence imaging without intermediate exposures to films or screens" (see sixth bullet).

Response to Arguments

In prior Office Action, claims 13-21 were rejected under 35 U.S.C. 103(a) as being unpatentable over various combinations of teachings from Ro et al., 126 PLANT PHYSIOL. 317 (2001), Kay (US 3,789,116), Einhauer & Jungbauer, 49 J. BIOCHEM. BIOPHYS. METHODS 455 (2001), and Amersham Biosciences, Application Note 80-6443-83 (1999). In response, Applicant amends claim 13 to add the step of "quantifying". These rejections are withdrawn in light of Applicant's amendment, and in light of new claim rejections in view of Yabusaki et al., set forth supra. Further discussion pertaining to the teachings of Ro et al. has been rendered moot.

With respect to the teachings of Kay, Applicant argues there is no teaching or suggestion that Kay could be used in western blot analysis to quantitate low levels of proteins, and that persons skilled in the art of the protein sciences in 1974 would understand that Kay only provides for qualitative testing (see Applicant's reply, p. 7, first full paragraph), and that the cited prior art do not possess the limits of detection that Applicant's invention achieves (see Applicant's reply, p. 7, second full paragraph). These arguments are not persuasive because, Examiner posits, persons skilled in the art *at the time of invention in 2002* would readily appreciate the sensitivity of fluorescence-based assays using fluorophore-conjugated antibodies, as Kay discloses such antibody reagents having "superior sensitivity" (see col. 1, line 66) and "excellent fluorescent characteristics including both brightness and color" (see col. 2, lines 20-24).

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Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv



LONG V. LE
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11/14/01